

AMENDMENTS**Amendments to the Claims**

1. (Currently amended) A method of predicting or determining immuno-resistance to botulinum toxin therapy in an individual, the method comprising the step of determining the presence or absence in said individual of antibodies immunoreactive with a BoNT/A peptide comprising amino acids 785-803 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof and at least one additional BoNT/A peptide, said additional BoNT/A peptide comprising the amino acid sequence~~with two or more amino acid sequences~~ selected from the group consisting of~~[[:]]~~ 785-803 of SEQ ID NO: 1 [N25]; amino acids 981-999 of SEQ ID NO: 1, [C10]; amino acids 1051-1069 of SEQ ID NO: 1, [C15]; amino acids 1121-1139 of SEQ ID NO: 1, [C20]; and amino acids 1275-1296 of SEQ ID NO: 1 [C34], or a conservative BoNT/A amino acid sequence variant thereof or and an immunoreactive BoNT/A amino acid sequence fragment thereof

wherein said antibodies immunoreact with amino acids 785-803 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof and an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1, or 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1;

wherein said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said antibodies comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-

1139 of SEQ ID NO: 1 or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1; and

wherein the presence of antibodies immunoreactive with at least one of said BoNT/A peptides ~~two or more amino acid sequences~~ indicates immuno-resistance to a botulinum toxin therapy.

2. (Currently amended) The method of claim 1, wherein each of said amino acid sequences of said additional BoNT/A peptides ~~amino acid sequences are~~ is selected from the group consisting of ~~of~~ 785-803 of SEQ ID NO: 1 [N25]; amino acids 981-999 of SEQ ID NO: 1, [C10]; amino acids 1051-1069 of SEQ ID NO: 1, [C15]; amino acids 1121-1139 of SEQ ID NO: 1, [C20]; and amino acids 1275-1296 of SEQ ID NO: 1-[C31], or and a conservative BoNT/A amino acid sequence variant thereof

wherein said conservative BoNT/A amino acid sequence variant immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1, or 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1.

3. (Currently amended) The method of claim 1, wherein each of said amino acid sequences of said additional BoNT/A peptides ~~amino acid sequences are~~ is selected from the group consisting of ~~of~~ 785-803 of SEQ ID NO: 1 [N25]; amino acids 981-999 of SEQ ID NO: 1, [C10]; amino acids 1051-1069 of SEQ ID NO: 1, [C15]; amino acids 1121-1139 of SEQ ID NO: 1, [C20]; and amino acids 1275-1296 of SEQ ID NO: 1-[C31], or and an immunoreactive BoNT/A amino acid sequence fragment thereof

wherein said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said antibodies comprises at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1, or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

4. (Currently amended) The method of claim 1, wherein each of said amino acid sequences of said additional BoNT/A peptides ~~amino acid sequences are~~ is selected from the group consisting of ~~[[:]] 785-803 of SEQ ID NO: 1 [N25];~~ amino acids 981-999 of SEQ ID NO: 1, [C10]; amino acids 1051-1069 of SEQ ID NO: 1, [C15]; amino acids 1121-1139 of SEQ ID NO: 1, [C20]; and amino acids 1275-1296 of SEQ ID NO: 1 [C31].
5. (Currently amended) The method of claim 1, wherein one of said amino acid sequences of said additional BoNT/A peptides ~~amino acid sequences comprises the amino acid sequence~~ is amino acids 981-999 of SEQ ID NO:1, 785-803 of SEQ ID NO: 1 [N25] or a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof

wherein said conservative BoNT/A amino acid sequence variant of amino acids 981-999 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1.

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 981-999 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 981-999 of SEQ ID NO: 1.

6. (Currently amended) The method of claim 1, ~~comprising determining the presence or absence in said individual of antibodies immunoreactive with the following two amino acid sequences: wherein one of said amino acid sequences of said additional BoNT/A peptides~~ is amino acids 1051-1069 of SEQ ID NO: 1 785-803 of SEQ ID NO: 1 [N25]; and 981-999 of SEQ ID NO: 1 [C10], or a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof

wherein said conservative BoNT/A amino acid sequence variant of amino acids 1051-1069 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1.

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1051-1069 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1.

7. (Currently amended) The method of ~~claim 6~~ claim 1, ~~comprising determining the presence or absence in said individual of antibodies immunoreactive with the following two amino acid sequences: wherein one of said amino acid sequences of said additional BoNT/A peptides is amino acids 1121-1139 of SEQ ID NO: 1, 785-803 of SEQ ID NO: 1 [N25]; and 981-999 of SEQ ID NO: 1 [C10], or a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof~~

wherein said conservative BoNT/A amino acid sequence variant of amino acids 1121-1139 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1121-1139 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1.

8. (Currently amended) The method of ~~claim 6~~ claim 1, ~~comprising determining the presence or absence in said individual of antibodies immunoreactive with the following two amino acid sequences: wherein one of said amino acid sequences of said additional BoNT/A peptides is amino acids 1275-1296 of SEQ ID NO: 1, 785-803 of SEQ ID NO: 1 [N25]; and 981-999 of SEQ ID NO: 1 [C10], a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof~~

wherein said conservative BoNT/A amino acid sequence variant of amino acids 1275-1296 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1275-1296 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

9. (Currently amended) The method of ~~claim 6~~ claim 1, ~~comprising determining the presence or absence in said individual of antibodies immunoreactive with the following two amino acid sequences: wherein two of said amino acid sequences of said additional BoNT/A peptides are amino acids 785-803 of SEQ ID NO: 1 [N25]; and 981-999 of SEQ ID NO: 1-[C10], amino acids 1051-1069 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof~~

wherein said conservative BoNT/A amino acid sequence variant immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1 or 1-4 conservative amino acid substitutions to amino acids 1051-1069; and

wherein said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said antibodies comprises at least six consecutive amino acids of 981-999 of SEQ ID NO: 1 or at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1.

10. (Currently amended) The method of ~~claim 1~~, ~~comprising determining the presence or absence in said individual of antibodies immunoreactive with the following three amino acid sequences: wherein two of said amino acid sequences of said additional BoNT/A peptides are amino acids 785-803 of SEQ ID NO: 1 [N25]; 981-999 of SEQ ID NO: 1-[C10]; and amino acids 1121-1139 1051-1069 of SEQ ID NO: 1-[C15], or a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof~~

wherein said conservative BoNT/A amino acid sequence variant immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1 or 1-4 conservative amino acid substitutions to amino acids 1121-1139; and

wherein said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said antibodies comprises at least six consecutive amino acids of 981-999 of SEQ ID NO: 1 or at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1.

11. (Currently amended) ~~The method of claim 10, comprising determining the presence or absence in said individual of antibodies immunoreactive with the following three amino acid sequences: wherein two of said amino acid sequences of said additional BoNT/A peptides are amino acids 785-803 of SEQ ID NO: 1 [N25]; 981-999 of SEQ ID NO: 1 [C10]; and amino acids 1275-1296 1051-1069 of SEQ ID NO: 1 [C15], or a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof~~

wherein said conservative BoNT/A amino acid sequence variant immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1 or 1-4 conservative amino acid substitutions to amino acids 1275-1296; and

wherein said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said antibodies comprises at least six consecutive amino acids of 981-999 of SEQ ID NO: 1 or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

12. (Currently amended) ~~A The method of claim 10, comprising determining the presence or absence in said individual of antibodies immunoreactive with the following three amino acid sequences: 785-803 of SEQ ID NO: 1 [N25]; 981-999 of SEQ ID NO: 1 [C10]; and 1051-1069 of SEQ ID NO: 1 [C15], or an immunoreactive fragment thereof predicting or determining immuno-resistance to botulinum toxin therapy in an individual, the method comprising the step of determining the presence or absence in said individual of antibodies immunoreactive with at least a BoNT/A peptide comprising amino acids 785-803 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof~~

wherein said antibodies immunoreact with amino acids 785-803 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof and an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant of amino acids 785-803 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1;

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 785-803 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1; and

wherein the presence of antibodies immunoreactive with said BoNT/A peptide indicates immuno-resistance to botulinum toxin therapy.

13. (Currently amended) The method of ~~claim 10~~ claim 12, ~~comprising determining the presence or absence in said individual of antibodies immunoreactive with the following three amino acid sequences: wherein said amino acid sequence of said BoNT/A peptide is amino acids 785-803 of SEQ ID NO: 1 [N25]; 981-999 of SEQ ID NO: 1, [C10]; and 1051-1069 of SEQ ID NO: 1 [C15].~~
14. (Currently amended) The method of claim ~~1, 6 or 10~~, comprising selectively determining the presence or absence in said individual of IgG antibodies immunoreactive with each of said ~~amino acid sequences~~ immunoreactive BoNT/A peptides.
15. (Currently amended) The method of claim ~~1 or 12, 6 or 10~~, wherein the presence or absence of antibodies immunoreactive with each of said ~~amino acid sequences~~ immunoreactive BoNT/A peptides is determined using an enzyme-linked immunosorbent assay.
16. (Currently amended) The method of claim ~~1 or 12, 6 or 10~~, wherein the presence or absence of antibodies immunoreactive with each of said ~~amino acid sequences~~ immunoreactive BoNT/A peptides is determined using a radioimmunoassay.
17. (Currently amended) The method of claim ~~1 or 12, 6 or 10~~, wherein said botulinum toxin therapy is BoNT/A therapy.
18. (Currently amended) A method of preventing or reducing immuno-resistance to botulinum toxin therapy in an individual, the method comprising the step of administering to said individual a tolerogizing composition comprising agent and two at least one or more amino

acid sequences BoNT/A peptide conjugated with a tolerogizing agent thereby preventing or reducing immuno-resistance to botulinum toxin therapy

wherein said BoNT/A peptide comprises an amino acid sequence selected from the group consisting of [[:]] amino acids 785-803 of SEQ ID NO: 1, [N25]; amino acids 981-999 of SEQ ID NO: 1, [C10]; amino acids 1051-1069 of SEQ ID NO: 1, [C15]; amino acids 1121-1139 of SEQ ID NO: 1, [C20]; and amino acids 1275-1296 of SEQ ID NO: 1, [C31], or a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive and a tolerogenic BoNT/A amino acid sequence fragment thereof, thereby preventing or reducing immuno-resistance to botulinum toxin therapy

wherein said amino acids 785-803 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof and a tolerogenic BoNT/A amino acid sequence fragment thereof produce a decrease in an immunological response;

wherein said conservative BoNT/A amino acid sequence variant producing a decreased immunological response comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1, or 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1; and

wherein said tolerogenic BoNT/A amino acid sequence fragment producing a decreased immunological response comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1 or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

19. (Currently amended) The tolerogizing method of claim 18, wherein said tolerogizing composition comprises at least two different BoNT/A peptides conjugated with a tolerogizing agent, said BoNT/A peptides comprising an amino acids sequence comprising administering to said individual a tolerogizing agent and two or more amino acid sequences selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1, [N25]; amino acids 981-999 of SEQ ID NO: 1, [C10]; amino acids 1051-1069 of SEQ ID NO: 1, [C15]; amino acids 1121-1139 of SEQ ID NO: 1, [C20]; and amino acids 1275-1296 of SEQ ID NO: 1, [C31], or a conservative BoNT/A amino acid sequence variant thereof and a tolerogenic BoNT/A amino acid sequence fragment thereof

wherein said conservative BoNT/A amino acid sequence variant producing a decreased immunological response comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1, or 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1; and

wherein said tolerogenic BoNT/A amino acid sequence fragment producing a decreased immunological response comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1 or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

20. (Currently amended) The tolerogizing method of claim 18, wherein said tolerogizing composition comprises at least three different BoNT/A peptides conjugated with a tolerogizing agent, said BoNT/A peptides comprising an amino acids sequence comprising administering to said individual a tolerogizing agent and two or more amino acid sequences selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1, [N25]; amino acids 981-999 of SEQ ID NO: 1, [C10]; amino acids 1051-1069 of SEQ ID NO: 1, [C15]; amino acids 1121-1139 of SEQ ID NO: 1, [C20]; and amino acids 1275-1296 of SEQ

ID NO: 1-[C34], ~~or~~ a conservative BoNT/A amino acid sequence variant thereof and an immunoreactive a tolerogenic BoNT/A amino acid sequence fragment thereof

wherein said conservative BoNT/A amino acid sequence variant producing a decreased immunological response comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1, or 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1; and

wherein said tolerogenic BoNT/A amino acid sequence fragment producing a decreased immunological response comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1 or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

21. (Currently amended) The tolerogizing method of claim 18, wherein said tolerogizing composition comprises at least four different BoNT/A peptides conjugated with a tolerogizing agent, said BoNT/A peptides comprising an amino acids sequence comprising administering to said individual a tolerogizing agent and two or more amino acid sequences selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1, [N25]; amino acids 981-999 of SEQ ID NO: 1, [C10]; amino acids 1051-1069 of SEQ ID NO: 1, [C15]; amino acids 1121-1139 of SEQ ID NO: 1, [C20]; and amino acids 1275-1296 of SEQ ID NO: 1, [C34], a conservative BoNT/A amino acid sequence variant thereof and a tolerogenic BoNT/A amino acid sequence fragment thereof

wherein said conservative BoNT/A peptide variant producing a decreased immunological response comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO:

1, 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1, or 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1; and

wherein said tolerogenic BoNT/A amino acid sequence fragment producing a decreased immunological response comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1 or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

22. (Currently amended) The tolerogizing method of claim 18, ~~comprising administering the following two amino acid sequences:~~ wherein two of said BoNT/A peptides comprise an amino acid sequence selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1, [N25]; and amino acids 981-999 of SEQ ID NO: 1-[C10], or a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive a tolerogenic BoNT/A amino acid sequence fragment thereof.

wherein said conservative BoNT/A amino acid sequence variant producing a decreased immunological response comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1 or 1-4 conservative amino acid substitutions to amino acids 981-999; and

wherein said tolerogenic BoNT/A amino acid sequence fragment producing a decreased immunological response comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1 or at least six consecutive amino acids of 981-999 of SEQ ID NO: 1.

23. (Currently amended) The tolerogizing method of claim 22, ~~comprising administering the following two amino acid sequences:~~ wherein two of said BoNT/A peptides comprise an amino acid sequence selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1, [N25]; and amino acids 981-999 of SEQ ID NO: 1-[C10], or a conservative BoNT/A amino acid sequence variant thereof

wherein said conservative BoNT/A amino acid sequence variant producing a decreased immunological response comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1 or 1-4 conservative amino acid substitutions to amino acids 981-999.

24. (Currently amended) The tolerogizing method of claim 22, ~~comprising administering the following two amino acid sequences: wherein two of said BoNT/A peptides comprise an amino acid sequence selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1-[N25]; and amino acids 981-999 of SEQ ID NO: 1-[C10], or an immunoreactive a tolerogenic BoNT/A amino acid sequence fragment thereof.~~

wherein said tolerogenic BoNT/A amino acid sequence fragment producing a decreased immunological response comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1 or at least six consecutive amino acids of 981-999 of SEQ ID NO: 1.

25. (Currently amended) The tolerogizing method of claim 22, ~~comprising administering the following two amino acid sequences: wherein two of said BoNT/A peptides are amino acids 785-803 of SEQ ID NO: 1-[N25]; and or amino acids 981-999 of SEQ ID NO: 1-[C10].~~

26. (Currently amended) The tolerogizing method of claim 18, ~~comprising administering the following three amino acid sequences: wherein two of said BoNT/A peptides comprise an amino acid sequence selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1-[N25]; amino acids 981-999 of SEQ ID NO: 1-[C10]; and amino acids 1051-1069 of SEQ ID NO: 1-[C16], or a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive a tolerogenic BoNT/A amino acid sequence fragment thereof.~~

wherein said conservative BoNT/A amino acid sequence variant producing a decreased immunological response comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 981-999 or 1-4 conservative amino acid substitutions to amino acids 1051-1069; and

wherein said tolerogenic BoNT/A amino acid sequence fragment comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1 producing a decreased immunological

response, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1 producing a decreased immunological response or at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1 producing a decreased immunological response.

27. (Currently amended) The tolerogizing method of claim 26, ~~comprising administering the following three amino acid sequences:~~ wherein three of said BoNT/A peptides comprise an amino acid sequence selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1, ~~[N25]~~; amino acids 981-999 of SEQ ID NO: 1, ~~[C10]~~; and amino acids 1051-1069 of SEQ ID NO: 1 ~~[C15]~~ or a conservative BoNT/A amino acid sequence variant thereof

wherein said conservative BoNT/A amino acid sequence variant producing a decreased immunological response comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 981-999 or 1-4 conservative amino acid substitutions to amino acids 1051-1069.

28. (Currently amended) The tolerogizing method of claim 26, ~~comprising administering the following three amino acid sequences:~~ wherein three of said BoNT/A peptides comprise an amino acid sequence selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1, ~~[N25]~~; amino acids 981-999 of SEQ ID NO: 1, ~~[C10]~~; and amino acids 1051-1069 of SEQ ID NO: 1 ~~[C15]~~, or an immunoreactive a tolerogenic BoNT/A amino acid sequence fragment thereof

wherein said tolerogenic BoNT/A amino acid sequence fragment producing a decreased immunological response comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1 or at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1.

29. (Currently amended) The tolerogizing method of claim 26, ~~comprising administering the following three amino acid sequences:~~ wherein three of said BoNT/A peptides comprise an amino acid sequence selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1, ~~[N25]~~; amino acids 981-999 of SEQ ID NO: 1, ~~[C10]~~; and amino acids 1051-1069 of SEQ ID NO: 1 ~~[C15]~~.

30. (Currently amended) The tolerogizing method of claim 18, 22 or 26, wherein said botulinum toxin therapy is BoNT/A therapy.

31. (Currently amended) A method of inducing an immune response in ~~vaccinating~~ an individual ~~against botulinum toxin~~, the method comprising the step of administering to said individual a vaccine composition thereby producing an immune response in said individual

wherein said composition comprises ~~comprising~~ an adjuvant, a BoNT/A peptide comprising amino acids 785-803 of SEQ ID NO: 1 and at least one additional BoNT/A peptide, said additional BoNT/A peptide comprising an amino acid sequence ~~with two or more amino acid sequences~~ selected from the group consisting of ~~785-803 of SEQ ID NO: 1 [N25]; amino acids 981-999 of SEQ ID NO: 1, [C10]; amino acids 1051-1069 of SEQ ID NO: 1, [C15]; amino acids 1121-1139 of SEQ ID NO: 1, [C20]; and amino acids 1275-1296 of SEQ ID NO: 1, [C31]; or a conservative variant~~ or and an immunoreactive BoNT/A amino acid sequence fragment thereof, ~~thereby producing an immune response to said botulinum toxin in said individual.~~

wherein said amino acids 785-803 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1 and an immunoreactive BoNT/A amino acid sequence fragment thereof produce an immune response; and

wherein said immunoreactive BoNT/A amino acid sequence fragment producing an immune response comprises at least eight consecutive amino acids of 785-803 of SEQ ID NO: 1, at least eight consecutive amino acids of 981-999 of SEQ ID NO: 1, at least eight consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least eight consecutive amino acids of 1121-1139 of SEQ ID NO: 1 or at least eight consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

32. (Currently amended) The method of claim 31, ~~comprising administering to said individual a vaccine comprising an adjuvant and two or more amino acid sequences selected from the group; wherein said additional BoNT/A peptide comprises an amino acid sequence selected from the group consisting of~~ 785-803 of SEQ ID NO: 1 [N25]; 981-999 of SEQ ID NO: 1,

~~[C10]; amino acids 1051-1069 of SEQ ID NO: 1, [C15]; amino acids 1121-1139 of SEQ ID NO: 1, [C20]; and amino acids 1275-1296 of SEQ ID NO: 1 [C31], or a conservative variant thereof.~~

33. (Currently amended) The method of claim 31, ~~comprising administering to said individual a vaccine comprising an adjuvant and two or more amino acid sequences selected from the group: wherein one of said additional BoNT/A peptides comprise the amino acid sequence selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1 [N25]; 981-999 of SEQ ID NO: 1 [C10]; 1051-1069 of SEQ ID NO: 1 [C15]; 1121-1139 of SEQ ID NO: 1 [C20]; and 1275-1296 of SEQ ID NO: 1 [C31], or and an immunoreactive BoNT/A amino acid sequence~~ fragment thereof

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 981-999 of SEQ ID NO:1 producing an immune response comprises at least eight consecutive amino acids of 981-999 of SEQ ID NO: 1.

34. (Currently amended) The method of claim 31, ~~comprising administering to said individual a vaccine comprising an adjuvant and two or more amino acid sequences selected from the group: wherein one of said additional BoNT/A peptides comprise the amino acid sequence selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1 [N25]; 981-999 of SEQ ID NO: 1 [C10]; 1051-1069 of SEQ ID NO: 1 [C15]; 1121-1139 of SEQ ID NO: 1 [C20]; and 1275-1296 of SEQ ID NO: 1 [C31] and an immunoreactive BoNT/A amino acid sequence~~ fragment thereof

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1051-1069 of SEQ ID NO:1 producing an immune response comprises at least eight consecutive amino acids of 1051-1069 of SEQ ID NO: 1.

35. (Currently amended) The method of claim 31, ~~wherein one of said amino acid sequences comprises residues 785-803 of SEQ ID NO: 1 [N25] or a conservative variant or an immunoreactive fragment thereof. wherein one of said additional BoNT/A peptides comprise the amino acid sequence selected from the group consisting of amino acids 1275-1296 of SEQ ID NO: 1 and an immunoreactive BoNT/A amino acid sequence~~ fragment thereof

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1275-1296 of SEQ ID NO:1 producing an immune response comprises at least eight consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

36. (Currently amended) The method of claim 31, ~~comprising administering to said individual a vaccine comprising an adjuvant and the following two amino acid sequences:-~~ wherein two of said additional BoNT/A peptides comprise the amino acid sequence selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1, [N25]; and amino acids 981-999 of SEQ ID NO: 1 [C10], or a conservative variant or an immunoreactive fragment thereof.
37. (Currently amended) The method of claim 31, ~~comprising administering to said individual a vaccine comprising an adjuvant and the following two amino acid sequences:-~~ wherein two of said additional BoNT/A peptides comprise the amino acid sequence selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1, [N25]; and amino acids 1051-1069 of SEQ ID NO: 1-981-999 of SEQ ID NO: 1 [C10], or a conservative variant thereof.
38. (Currently amended) The method of claim 31, ~~comprising administering to said individual a vaccine comprising an adjuvant and the following two amino acid sequences:-~~ wherein two of said additional BoNT/A peptides comprise the amino acid sequence selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1, [N25]; and amino acids 1121-1139 of SEQ ID NO: 1-981-999 of SEQ ID NO: 1 [C10], or and an immunoreactive fragment thereof.
39. (Currently amended) The method of claim 31, ~~comprising administering to said individual a vaccine comprising an adjuvant and the following two amino acid sequences:-~~ wherein two of said additional BoNT/A peptides comprise the amino acid sequence selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1, [N25]; and amino acids 1275-1296 of SEQ ID NO: 1-981-999 of SEQ ID NO: 1 [C10].
40. (Currently amended) The method of claim 31, ~~comprising administering to said individual a vaccine comprising an adjuvant and the following three amino acid sequences:-~~ wherein three of said additional BoNT/A peptides comprise the amino acid sequence selected from

the group consisting of amino acids 785-803 of SEQ ID NO: 1, [N25]; amino acids 981-999 of SEQ ID NO: 1, [C10]; and amino acids 1051-1069 of SEQ ID NO: 1, [C15], or a conservative variant or an immunoreactive fragment thereof.

41. (Currently amended) The method of claim 31, ~~comprising administering to said individual a vaccine comprising an adjuvant and the following three amino acid sequences: wherein~~ three of said additional BoNT/A peptides comprise the amino acid sequence selected from the group consisting of amino acids 981-999 of SEQ ID NO: 1, [C10]; and amino acids 1121-1139 of SEQ ID NO: 1, [C15], or conservative variant thereof.
42. (Currently amended) The method of claim 31, ~~comprising administering to said individual a vaccine comprising an adjuvant and the following three amino acid sequences: wherein~~ three of said additional BoNT/A peptides comprise the amino acid sequence selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1, [N25]; amino acids 981-999 of SEQ ID NO: 1, [C10]; and amino acids 1275-1296 of SEQ ID NO: 1, [C15], or an immunoreactive fragment thereof.
43. (Currently amended) The method of claim 31, ~~comprising administering to said individual a vaccine comprising an adjuvant and the following three amino acid sequences: wherein four~~ of said additional BoNT/A peptides comprise the amino acid sequence selected from the group consisting of amino acids 981-999 of SEQ ID NO: 1, [C10]; and amino acids 1051-1069 of SEQ ID NO: 1, [C15] and amino acids 1275-1296 of SEQ ID NO: 1.
44. (Currently amended) A method of removing botulinum toxin blocking antibodies from an individual, patient, the method comprising the steps of
 - (a) removing blood from a said individual patient;
 - (b) contacting said blood, or an antibody-containing component thereof, with at least one BoNT/A peptide, said BoNT/A peptide comprising an amino acid sequence two or more amino acid sequences selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1, [N25]; amino acids 981-999 of SEQ ID NO: 1, [C10]; amino acids 1051-1069 of SEQ ID NO: 1, [C15]; amino acids 1121-1139 of SEQ ID NO: 1, [C20]; and

amino acids 1275-1296 of SEQ ID NO: 1-[C31], or a conservative BoNT/A amino acid sequence variant thereof or and an immunoreactive BoNT/A amino acid sequence fragment thereof, under conditions suitable for forming a complex of at least one BoNT/A peptide each of said amino acid sequences and anti-botulinum toxin antibody; and

wherein said anti-botulinum toxin antibody complexes with amino acids 785-803 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant immunoreactive with said anti-botulinum toxin antibody comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1 or 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said anti-botulinum toxin antibody comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1 or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1;

(c) removing said complex from said blood or antibody-containing component thereof[.]]
thereby forming antibody-depleted blood; and

(d) returning said antibody-depleted blood to said individual.

45. (Currently amended) The method of claim 44, wherein step (b) comprises contacting said blood, or an antibody-containing component thereof, with two ~~the following two amino acid~~

sequences ~~BoNT/A peptides, said BoNT/A peptides comprising an amino acid sequence~~ selected from the group consisting of ~~[[:]]~~ 785-803 of SEQ ID NO: 1, ~~[N25]~~, and 981-999 of SEQ ID NO: 1 ~~[C10]~~, or a conservative BoNT/A amino acid sequence variant thereof or and an immunoreactive BoNT/A amino acid sequence fragment thereof

wherein said conservative BoNT/A amino acid sequence variant immunoreactive with said antibody comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1 or 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said antibody comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1 or at least six consecutive amino acids of 981-999 of SEQ ID NO: 1.

46. (Currently amended) The method of claim 44, wherein step (b) comprises contacting said blood, or an antibody-containing component thereof, with three the following three amino acid sequencesBoNT/A peptides, said BoNT/A peptides comprising an amino acid sequence selected from the group consisting of ~~[[:]]~~ 785-803 of SEQ ID NO: 1, ~~[N25]~~; 981-999 of SEQ ID NO: 1, ~~[C10]~~; and 1051-1069 of SEQ ID NO: 1 ~~[C15]~~, or a conservative BoNT/A amino acid sequence variant thereof or and an immunoreactive BoNT/A amino acid sequence fragment thereof

wherein said conservative BoNT/A amino acid sequence variant immunoreactive with said antibody comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1 or 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said antibody comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1 or at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1.

47. (Currently amended) The method of claim 44, 45 or 46, comprising selectively removing IgG botulinum toxin blocking antibodies from said individual ~~patient~~.

48. (Currently amended) A method of predicting or determining immuno-resistance to botulinum toxin therapy in an individual, the method comprising the steps of:

(a) determining the level of IgG antibodies immunoreactive with at least one BoNT/A peptide, said BoNT/A peptide comprising an amino acid sequence selected from the group consisting of amino acids 785-803 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof and an immunoreactive BoNT/A amino acid sequence fragment thereof ~~said botulinum toxin in said individual; and~~

wherein said IgG antibodies immunoreact with amino acids 785-803 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant immunoreactive with said IgG antibodies comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1 or 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1; and

wherein said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said IgG antibodies comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive

amino acids of 1121-1139 of SEQ ID NO: 1 or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1; and

(b) comparing said level of IgG antibodies to a control level of IgG antibodies[[,]];]

wherein an increase in said level of IgG antibodies in said individual as compared to said control level indicates immunoresistance to said botulinum toxin therapy.

49. (Original) The method of claim 48, wherein said increase is at least a 5-fold increase.

50. (Original) The method of claim 48, wherein said increase is at least a 10-fold increase.

51. (Original) The method of claim 48, wherein said control level of IgG antibodies is determined in an individual who has not been treated with botulinum toxin therapy.

52. (Original) The method of claim 48, wherein said control level of IgG antibodies is determined in an individual who is responsive to said botulinum toxin therapy.

53. (Currently amended) The method of claim 48, wherein said botulinum toxin therapy is a BoNT/A therapy.

54. (Currently amended) A method of predicting or determining immunoresistance to botulinum toxin therapy in an individual, the method comprising the step of determining the presence or absence in said individual of antibodies immunoreactive with a BoNT/A peptide of SEQ ID NO: 1 having a length of at most 60 amino acids ~~and comprising amino acid sequence selected from the group : 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a conservative variant or immunoreactive fragment thereof~~

wherein said antibodies immunoreact with an amino acid sequence from said BoNT/A peptide, said amino acid sequence comprising amino acids 785-803 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant of amino acids 785-803 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1;

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 785-803 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1; and

wherein the presence of antibodies immunoreactive with said BoNT/A peptide indicates immuno-resistance to a botulinum toxin therapy, ~~and with the proviso that said BoNT/A peptide is not SEQ ID NO:2.~~

55. (Currently amended) The method of claim 54, ~~wherein said BoNT/A peptide comprises an amino acid sequence selected from the group: 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, and 823-849 of SEQ ID NO:1, or a conservative variant or immunoreactive fragment thereof, with the proviso that said BoNT/A peptide is not SEQ ID NO:2~~ further comprising at least one additional BoNT/A peptide of SEQ ID NO: 1, said additional BoNT/A peptides having a length of at most 60 amino acids

wherein said antibodies immunoreact with and comprising an amino acid sequence of said additional BoNT/A peptides, said amino acid sequence selected from the group consisting of ~~[[:]] 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of~~

~~SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-836 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a conservative variant or immunoreactive fragment thereof~~ amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1 and amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof;

wherein said conservative BoNT/A amino acid sequence variant immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1, or 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1;

wherein said immunoreactive BoNT/A amino acid sequence fragment immunoreactive with said antibodies comprises at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1 or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1; and

wherein the presence of antibodies immunoreactive with at least one of said additional BoNT/A peptides indicates immunoresistance to a botulinum toxin therapy, ~~and with the proviso that said BoNT/A peptide is not SEQ ID NO:2.~~

56. (Currently amended) The method of claim 54, wherein said BoNT/A peptide has a length of at most 40 amino acids.

57. (Currently amended) The method of ~~claim 54~~ claim 55, wherein said additional BoNT/A peptides ~~has~~ have a length of at most ~~25~~ 40 amino acids.

58. (Currently amended) The method of claim 54, wherein said amino acid sequence of said of said additional BoNT/A peptide immunoreactive with said antibodies ~~BoNT/A peptide~~ comprises an ~~amino acid sequence selected from the group: 445-471 of SEQ ID NO:1, 487-~~

~~513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a conservative variant thereof~~ amino acids 981-999 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof

wherein said conservative BoNT/A amino acid sequence variant of amino acids 981-999 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 981-999 of SEQ ID NO: 1.

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 981-999 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 981-999 of SEQ ID NO: 1.

59. (Currently amended) The method of claim 54, wherein said amino acid sequence of said of said additional BoNT/A peptide immunoreactive with said antibodies ~~BoNT/A peptide comprises an amino acid sequence selected from the group: 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or an immunoreactive fragment thereof, with the proviso that said BoNT/A peptide is not SEQ ID NO:2~~ amino acids 1051-1069 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof

wherein said conservative BoNT/A amino acid sequence variant of amino acids 1051-1069 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 1051-1069 of SEQ ID NO: 1.

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1051-1069 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1.

60. (Currently amended) The method of claim 54, wherein said amino acid sequence of said of said additional BoNT/A peptide immunoreactive with said antibodies ~~BoNT/A peptide comprises an amino acid sequence selected from the group: 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1~~ amino acids 1121-1139 of SEQ ID NO: 1, a conservative BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof

wherein said conservative BoNT/A amino acid sequence variant of amino acids 1121-1139 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 1121-1139 of SEQ ID NO: 1.

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1121-1139 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1.

61. (Currently amended) The method of claim 54, wherein said amino acid sequence of said of said additional BoNT/A peptide immunoreactive with said antibodies ~~BoNT/A peptide consists of an amino acid sequence selected from the group consisting of[[:]] 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1~~ comprises amino acids 1275-1296 of SEQ ID NO: 1, a conservative

BoNT/A amino acid sequence variant thereof or an immunoreactive BoNT/A amino acid sequence fragment thereof

wherein said conservative BoNT/A amino acid sequence variant of amino acids 1275-1296 of SEQ ID NO:1 immunoreactive with said antibodies comprises 1-4 conservative amino acid substitutions to amino acids 1275-1296 of SEQ ID NO: 1.

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1275-1296 of SEQ ID NO:1 immunoreactive with said antibodies comprises at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

62. (Canceled)

63. (Currently amended) The method of claim 54 or ~~claim 62~~ claim 55, comprising selectively determining the presence or absence ~~in said individual~~ of IgG antibody component antibodies from said antibodies immunoreactive with said amino acid sequences ~~BoNT/A peptide~~.

64-66. (Canceled)

67. (Currently amended) The method of ~~claim 54~~ claim 55, wherein the presence or absence of antibodies immunoreactive with two or more of said additional amino acid sequences ~~BoNT/A peptides~~ is determined.

68. (Currently amended) The method of ~~claim 54~~ claim 55, wherein the presence or absence of antibodies immunoreactive with ~~five~~ three or more of said additional amino acid sequences ~~BoNT/A peptides~~ is determined.

69. (Currently amended) The method of ~~claim 54~~ claim 55, wherein the presence or absence of antibodies immunoreactive with ~~ten~~ four ~~or more~~ of said additional amino acid sequences ~~BoNT/A peptides~~ is determined.

70. (Currently amended) The method of claim 54, 67, 68 or 69, wherein ~~each of~~ said BoNT/A peptide ~~[[s]]~~ is immobilized on a solid support.

71. (Currently amended) The method of ~~claim 54~~ claim 55, ~~wherein the presence or absence of antibodies immunoreactive with said BoNT/A peptides is determined using an enzyme-linked immunosorbent assay wherein said additional BoNT/A peptides are immobilized on a solid support.~~
72. (Currently amended) The method of claim 54 or 55, wherein the presence or absence of antibodies said immunoreactive antibodies ~~with said BoNT/A peptides~~ is determined using a radioimmunoassay or an enzyme-linked immunosorbent assay.
73. (Currently amended) The method of claim 54 or 55, wherein said botulinum toxin therapy is a BoNT/A therapy.
74. (Currently amended) A method of preventing or reducing immunoresistance to botulinum toxin therapy in an individual, the method comprising the step of administering to said individual a tolerogizing composition comprising agent and a BoNT/A peptide of SEQ ID NO: 1 conjugated with a tolerogizing agent thereby preventing or reducing immunoresistance to botulinum toxin therapy[.].

wherein said BoNT/A peptide has a length of at most 30 amino acids

wherein said BoNT/A peptide having a length of at most 60 amino acids and comprising comprises an amino acid sequence selected from the group consisting of[.:] 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a conservative variant or immunoreactive fragment thereof, thereby preventing or reducing immunoresistance to botulinum toxin therapy, with the proviso that said BoNT/A peptide is not SEQ ID NO:2 amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 869-887 of SEQ

ID NO: 1, amino acids 925-943 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 995-1013 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, , amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1135-1153 of SEQ ID NO: 1, amino acids 1177-1195 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1 and a tolerogenic BoNT/A amino acid sequence fragment thereof

wherein said amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 869-887 of SEQ ID NO: 1, amino acids 925-943 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 995-1013 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, , amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1135-1153 of SEQ ID NO: 1, amino acids 1177-1195 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1 and an tolerogenic BoNT/A amino acid sequence fragment thereof produce a decrease in an immunological response; and

wherein said tolerogenic BoNT/A amino acid sequence producing a decreased immunological response comprises at least six consecutive amino acids of 547-565 of SEQ ID NO: 1, at least six consecutive amino acids of 589-607 of SEQ ID NO: 1, at least six consecutive amino acids of 659-677 of SEQ ID NO: 1, at least six consecutive amino acids of 743-761 of SEQ ID NO: 1, at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 869-887 of SEQ ID NO: 1, at least six consecutive amino acids of 925-943 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 995-1013 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1, at least six consecutive amino acids of 1135-1153 of SEQ ID NO: 1, at least six consecutive amino acids of 1177-1195 of SEQ ID NO: 1 or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

75. (Currently amended) The tolerogizing method of claim 74, wherein said BoNT/A peptide has a length of at most 40 amino acids comprises an amino acid sequence selected from the group consisting of amino acids 547-565 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 869-887 of SEQ ID NO: 1, amino acids 925-943 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 995-1013 of SEQ ID NO: 1, amino acids 1051-

1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1 and a tolerogenic BoNT/A amino acid sequence fragment thereof

wherein said tolerogenic BoNT/A amino acid sequence producing a decreased immunological response comprises at least six consecutive amino acids of 547-565 of SEQ ID NO: 1, at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 869-887 of SEQ ID NO: 1, at least six consecutive amino acids of 925-943 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 995-1013 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1 or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

76. (Currently amended) The tolerogizing method of claim 74 or 75, wherein said BoNT/A peptide has a length of at most 25 amino acids.

77. (Currently amended) The tolerogizing method of claim 74, wherein said BoNT/A peptide comprises an amino acid sequence selected from the group consisting of ~~445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a conservative variant thereof~~ amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 869-887 of SEQ ID NO: 1, amino acids 925-943 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 995-1013 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1135-1153 of SEQ ID NO: 1, amino acids 1177-1195 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1 and a tolerogenic BoNT/A amino acid sequence fragment thereof.

wherein said tolerogenic BoNT/A amino acid sequence producing a decreased immunological response comprises at least six consecutive amino acids of 547-565 of SEQ ID NO: 1, at least six consecutive amino acids of 589-607 of SEQ ID NO: 1, at least six consecutive amino acids of 659-677 of SEQ ID NO: 1, at least six consecutive amino acids of 743-761 of SEQ ID NO: 1, at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 869-887 of SEQ ID NO: 1, at least six consecutive amino acids of 925-943 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 995-1013 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1, at least six consecutive amino acids of 1135-1153 of SEQ ID NO: 1, at least six consecutive amino acids of 1177-1195 of SEQ ID NO: 1 or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

78. (Currently amended) The tolerogizing method of claim 74, wherein said BoNT/A peptide comprises an amino acid sequence selected from the group consisting of ~~of~~ 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or an immunoreactive fragment thereof, with the proviso that said BoNT/A peptide is not SEQ ID NO:2 amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 869-887 of SEQ ID NO: 1, amino acids 925-943 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 995-1013 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, , amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1135-1153 of SEQ ID NO: 1, amino acids 1177-1195 of SEQ ID NO: 1 and amino acids 1275-1296 of SEQ ID NO: 1.

79. (Currently amended) The tolerogizing method of ~~claim 74~~ claim 75, wherein said BoNT/A peptide comprises an amino acid sequence selected from the group consisting of ~~of~~ 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1,

~~599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1~~ amino acids 547-565 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 869-887 of SEQ ID NO: 1, amino acids 925-943 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 995-1013 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1.

80. (Canceled)

81. (Currently amended) The tolerogizing method of claim 74 or 75, wherein said BoNT/A peptide comprises the amino acid sequence of ~~residues~~ amino acids 785-803 of SEQ ID NO: 1 or a ~~conservative variant or immunoreactive~~ tolerogenic BoNT/A amino acid sequence fragment thereof

wherein said tolerogenic BoNT/A amino acid sequence fragment of amino acids 785-803 of SEQ ID NO: 1 comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1 producing a decreased immunological response.

82. (Currently amended) The tolerogizing method of claim 74 or 75, wherein said tolerogizing composition is agent and BoNT/A peptide are administered prior to said individual receiving botulinum toxin therapy.

83. (Currently amended) The tolerogizing method of claim 82, wherein said individual is at increased risk for immuno-resistance to a botulinum toxin therapy.

84-92. (Canceled)

93. (Currently amended) A BoNT/A peptide of SEQ ID NO: 1 having a length of at most 30 amino acids, said BoNT/A peptide~~[[,]]~~ comprising an amino acid sequence selected from the group consisting of~~[[:]]~~ ~~445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1,~~

~~585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a conservative variant or immunoreactive fragment thereof, said peptide having a length of at most 60 amino acids, with the proviso that said BoNT/A peptide is not SEQ ID NO:2~~ amino acids 491-509 of SEQ ID NO: 1, amino acids 519-537 of SEQ ID NO: 1, amino acids 533-551 of SEQ ID NO: 1, amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 631-649 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 673-691 of SEQ ID NO: 1, 715-733 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 771-789 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 813-831 of SEQ ID NO: 1, amino acids 827-845 of SEQ ID NO: 1 and a conservative BoNT/A amino acid sequence variant thereof

wherein said conservative BoNT/A amino acid sequence variant comprises 1-4 conservative amino acid substitutions to amino acids 491-509 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 519-537 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 533-551 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 547-565 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 589-607 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 631-649 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 659-677 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 673-691 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 715-733 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 743-761 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 771-789 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 813-831 or 1-4 conservative amino acid substitutions to amino acids 827-845 of SEQ ID NO: 1.

94. (Currently amended) The BoNT/A peptide of claim 93, comprising an amino acid sequence selected from the group consisting of~~[[:]]~~ ~~515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 739-~~

~~765 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, and 823-849 of SEQ ID NO:1, or a conservative variant or immunoreactive fragment thereof, with the proviso that said BoNT/A peptide is not SEQ ID NO:2~~ amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1 and a conservative BoNT/A amino acid sequence variant thereof

wherein said conservative BoNT/A amino acid sequence variant comprises 1-4 conservative amino acid substitutions to amino acids 547-565 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 589-607 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 659-677 of SEQ ID NO: 1, 1-4 conservative amino acid substitutions to amino acids 743-761 of SEQ ID NO: 1 or 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1.

95. (Canceled)

96. (Currently amended) The BoNT/A peptide of claim 93 or 94, having a length of at most 25 amino acids.

97. (Currently amended) The BoNT/A peptide of claim 93, comprising ~~which comprises an amino acid sequence selected from the group consisting of~~ ~~445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a conservative variant thereof~~ amino acids 547-565 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1 and a conservative BoNT/A amino acid sequence variant thereof

wherein said conservative BoNT/A amino acid sequence variant comprises 1-4 conservative amino acid substitutions to amino acids 547-565 of SEQ ID NO: 1 or 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1.

98. (Currently amended) The BoNT/A peptide of claim 93, comprising amino acids 659-677 of SEQ ID NO: 1 or a conservative BoNT/A amino acid sequence variant thereof ~~which comprises an amino acid sequence selected from the group: 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or an immunoreactive fragment thereof, with the proviso that said BoNT/A peptide is not SEQ ID NO:2.~~

wherein said conservative BoNT/A amino acid sequence variant of amino acids 659-677 of SEQ ID NO: 1 comprises 1-4 conservative amino acid substitutions to amino acids 659-677 of SEQ ID NO: 1.

99. (Currently amended) The BoNT/A peptide of claim 93, comprising amino acids 743-761 of SEQ ID NO: 1 or a conservative BoNT/A amino acid sequence variant thereof ~~which comprises an amino acid sequence selected from the group: 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1.~~

wherein said conservative BoNT/A amino acid sequence variant of amino acids 743-761 of SEQ ID NO: 1 comprises 1-4 conservative amino acid substitutions to amino acids 743-761 of SEQ ID NO: 1.

100. (Currently amended) The BoNT/A peptide of claim 93, comprising amino acids 547-565 of SEQ ID NO: 1 or a conservative BoNT/A amino acid sequence variant thereof ~~which consists of an amino acid sequence selected from the group: 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1.~~

~~NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1.~~

wherein said conservative BoNT/A amino acid sequence variant of amino acids 547-565 of SEQ ID NO: 1 comprises 1-4 conservative amino acid substitutions to amino acids 547-565 of SEQ ID NO: 1.

101. (Currently amended) The BoNT/A peptide of claim 93, ~~which comprises the amino acid sequence of residues comprising amino acids 785-803 of SEQ ID NO: 1 or a conservative BoNT/A amino acid sequence variant thereof or immunoreactive fragment thereof.~~

wherein said conservative BoNT/A amino acid sequence variant of amino acids 785-803 of SEQ ID NO: 1 comprises 1-4 conservative amino acid substitutions to amino acids 785-803 of SEQ ID NO: 1.

102. (Currently amended) A tolerogizing composition~~[[,]]~~ comprising a BoNT/A peptide of SEQ ID NO: 1 conjugated with a tolerogizing agent~~tolerogizing agent and a~~

wherein said BoNT/A peptide has a length of at most 30 amino acids;

wherein said BoNT/A peptide comprises ~~comprising an amino acid sequence selected from the group consisting of~~[[,:]]~~ 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a conservative variant or tolerogenic fragment thereof, said peptide having a length of at most 60 amino acids, with the proviso that said BoNT/A peptide is not~~ SEQ ID NO:2 amino acids 449-467 of SEQ ID NO: 1, amino acids 491-509 of SEQ ID NO: 1, amino acids 519-537 of SEQ ID NO: 1, amino acids 533-551 of SEQ ID NO: 1, amino acids 547-565 of SEQ ID NO: 1,

amino acids 589-607 of SEQ ID NO: 1, amino acids 631-649 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 673-691 of SEQ ID NO: 1, 715-733 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 771-789 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 813-831 of SEQ ID NO: 1, amino acids 827-845 of SEQ ID NO: 1, amino acids 869-887 of SEQ ID NO: 1, amino acids 911-929 of SEQ ID NO: 1, amino acids 925-943 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 995-1013 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1135-1153 of SEQ ID NO: 1, amino acids 1177-1195 of SEQ ID NO: 1, amino acids 1247-1265 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1 and a tolerogenic BoNT/A amino acid sequence fragment thereof

wherein said amino acids 449-467 of SEQ ID NO: 1, amino acids 491-509 of SEQ ID NO: 1, amino acids 519-537 of SEQ ID NO: 1, amino acids 533-551 of SEQ ID NO: 1, amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 631-649 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 673-691 of SEQ ID NO: 1, 715-733 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 771-789 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 813-831 of SEQ ID NO: 1, amino acids 827-845 of SEQ ID NO: 1, amino acids 869-887 of SEQ ID NO: 1, amino acids 911-929 of SEQ ID NO: 1, amino acids 925-943 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 995-1013 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1135-1153 of SEQ ID NO: 1, amino acids 1177-1195 of SEQ ID NO: 1, amino acids 1247-1265 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1 and a tolerogenic BoNT/A amino acid sequence fragment thereof produce a decrease in an immunological response; and

wherein said tolerogenic BoNT/A amino acid sequence fragment producing a decreased immunological response comprises at least six consecutive amino acids of 449-467 of SEQ ID NO: 1, at least six consecutive amino acids of 491-509 of SEQ ID NO: 1, at least six consecutive amino acids of 519-537 of SEQ ID NO: 1, at least six consecutive amino acids of 533-551 of SEQ ID NO: 1, at least six consecutive amino acids of 547-565 of SEQ ID NO: 1, at least six consecutive amino acids of 589-607 of SEQ ID NO: 1, at least six

consecutive amino acids of 631-649 of SEQ ID NO: 1, at least six consecutive amino acids of 659-677 of SEQ ID NO: 1, at least six consecutive amino acids of 673-691 of SEQ ID NO: 1, at least six consecutive amino acids of 715-733 of SEQ ID NO: 1, at least six consecutive amino acids of 743-761 of SEQ ID NO: 1, at least six consecutive amino acids of 771-789 of SEQ ID NO: 1, at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 813-831 of SEQ ID NO: 1, at least six consecutive amino acids of 827-845 of SEQ ID NO: 1, at least six consecutive amino acids of 869-887 of SEQ ID NO: 1, at least six consecutive amino acids of 911-929 of SEQ ID NO: 1, at least six consecutive amino acids of 925-943 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 995-1013 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1, at least six consecutive amino acids of 1135-1153 of SEQ ID NO: 1, at least six consecutive amino acids of 1177-1195 of SEQ ID NO: 1, at least six consecutive amino acids of 1247-1265 of SEQ ID NO: 1 or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

103. (Currently amended) The tolerogizing composition of claim 102, wherein said BoNT/A peptide comprises an amino acid sequence selected from the group consisting of ~~515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, and 823-849 of SEQ ID NO:1, or a conservative variant or tolerogenic fragment thereof, with the proviso that said BoNT/A peptide is not~~ SEQ ID NO:2 amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 869-887 of SEQ ID NO: 1, amino acids 925-943 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 995-1013 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1135-1153 of SEQ ID NO: 1, amino acids 1177-1195 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1 and a tolerogenic BoNT/A amino acid sequence fragment thereof

wherein said tolerogenic BoNT/A amino acid sequence fragment producing a decreased immunological response comprises at least six consecutive amino acids of 547-565 of

SEQ ID NO: 1, at least six consecutive amino acids of 589-607 of SEQ ID NO: 1, at least six consecutive amino acids of 659-677 of SEQ ID NO: 1, at least six consecutive amino acids of 743-761 of SEQ ID NO: 1, at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 869-887 of SEQ ID NO: 1, at least six consecutive amino acids of 925-943 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 995-1013 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1, at least six consecutive amino acids of 1135-1153 of SEQ ID NO: 1, at least six consecutive amino acids of 1177-1195 of SEQ ID NO: 1 or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

104. (Currently amended) The tolerogizing composition of claim 102, wherein said BoNT/A peptide ~~has a length of at most 40 amino acids~~ comprises an amino acid sequence selected from the group consisting of amino acids 547-565 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 869-887 of SEQ ID NO: 1, amino acids 925-943 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 995-1013 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1 and a tolerogenic BoNT/A amino acid sequence fragment thereof.

wherein said tolerogenic BoNT/A amino acid sequence fragment producing a decreased immunological response comprises at least six consecutive amino acids of 547-565 of SEQ ID NO: 1, at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 869-887 of SEQ ID NO: 1, at least six consecutive amino acids of 925-943 of SEQ ID NO: 1, at least six consecutive amino acids of 981-999 of SEQ ID NO: 1, at least six consecutive amino acids of 995-1013 of SEQ ID NO: 1, at least six consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least six consecutive amino acids of 1121-1139 of SEQ ID NO: 1 or at least six consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

105. (Currently amended) The tolerogizing composition of claim 102, wherein said BoNT/A peptide has a length of at most 25 amino acids.

106. (Currently amended) The tolerogizing composition of claim 102, wherein said BoNT/A peptide comprises an amino acid sequence selected from the group consisting of ~~of~~ 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a conservative variant thereof amino acids 449-467 of SEQ ID NO: 1, amino acids 491-509 of SEQ ID NO: 1, amino acids 519-537 of SEQ ID NO: 1, amino acids 533-551 of SEQ ID NO: 1, amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 631-649 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 673-691 of SEQ ID NO: 1, 715-733 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 771-789 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 813-831 of SEQ ID NO: 1, amino acids 827-845 of SEQ ID NO: 1, amino acids 869-887 of SEQ ID NO: 1, amino acids 911-929 of SEQ ID NO: 1, amino acids 925-943 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 995-1013 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1135-1153 of SEQ ID NO: 1, amino acids 1177-1195 of SEQ ID NO: 1, amino acids 1247-1265 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1.
107. (Currently amended) The tolerogizing composition of ~~claim 102-claim 103~~, wherein said BoNT/A peptide comprises an amino acid sequence selected from the group consisting of ~~of~~ 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a tolerogenic fragment thereof, with the proviso that said BoNT/A peptide is not SEQ ID NO:2 amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 869-887 of SEQ ID NO: 1, amino acids 925-943 of SEQ ID NO: 1, amino acids 981-999 of

SEQ ID NO: 1, amino acids 995-1013 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1135-1153 of SEQ ID NO: 1, amino acids 1177-1195 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1.

108. (Currently amended) The tolerogizing composition of ~~claim 102~~ claim 104, wherein said BoNT/A peptide comprises an amino acid sequence selected from the group consisting of ~~[[:]] 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1~~ amino acids 547-565 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 869-887 of SEQ ID NO: 1, amino acids 925-943 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 995-1013 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1.
109. (Currently amended) The tolerogizing composition of claim 102, wherein said BoNT/A peptide comprises ~~consists of~~ an amino acid sequence selected from the group consisting of ~~[[:]] 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1~~ amino acids 785-803 of SEQ ID NO: 1, amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1 and amino acids 1275-1296 of SEQ ID NO: 1.
110. (Currently amended) The tolerogizing composition of claim 102, wherein said BoNT/A peptide comprises the amino acid sequence of residues amino acids 785-803 of SEQ ID NO: 1 ~~or a conservative variant or immunoreactive~~ a tolerogenic BoNT/A amino acid sequence fragment thereof

wherein said tolerogenic BoNT/A amino acid sequence fragment of amino acids 785-803 of SEQ ID NO: 1 comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1 producing a decreased immunological response.

111. (Currently amended) The tolerogizing composition of claim 102, wherein said tolerogizing agent is polyethylene glycol (PEG).
112. (Currently amended) The tolerogizing composition of claim 102, wherein said tolerogizing agent is monomethoxypolyethylene glycol (mPEG).
113. (Currently amended) The tolerogizing composition of claim 102, wherein said tolerogizing agent is polyvinyl alcohol (PVA).
114. (Currently amended) An vaccine immune response inducing composition, comprising an adjuvant and a BoNT/A peptide of SEQ ID NO: 1, said BoNT/A peptide having a length of at most 60 amino acids comprising an amino acid sequence selected from the group: 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a conservative variant or immunoreactive fragment thereof, said peptide having a length of at most 60 amino acids, with the proviso that said BoNT/A peptide is not SEQ ID NO:2

wherein said BoNT/A peptide comprises an amino acid sequence capable of eliciting an immune response, said amino acid sequence comprising the amino acids 785-794 of SEQ ID NO: 1 or an immunoreactive BoNT/A amino acid sequence fragment thereof; and

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 785-794 of SEQ ID NO:1 producing an immune response comprises at least eight consecutive amino acids of 785-794 of SEQ ID NO: 1.

115. (Currently amended) The immune response inducing composition of claim 114, ~~wherein said BoNT/A peptide comprises an amino acid sequence selected from the group: 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, and 823-849 of SEQ ID NO:1 or a conservative variant or immunoreactive fragment thereof, with the proviso that said BoNT/A peptide is not SEQ ID NO:2~~ further comprising an additional BoNT/A peptide of SEQ ID NO: 1, said additional BoNT/A peptide having a length of at most 60 amino acids

wherein said additional BoNT/A peptide comprises an amino acid sequence capable of eliciting an immune response, said amino acid sequence selected from the group consisting of amino acids 981-999 of SEQ ID NO: 1, amino acids 1051-1069 of SEQ ID NO: 1, amino acids 1121-1139 of SEQ ID NO: 1, amino acids 1275-1296 of SEQ ID NO: 1 and an immunoreactive BoNT/A amino acid sequence fragment thereof.

wherein said immunoreactive BoNT/A amino acid sequence fragment producing an immune response comprises at least eight consecutive amino acids of 785-803 of SEQ ID NO: 1, at least eight consecutive amino acids of 981-999 of SEQ ID NO: 1, at least eight consecutive amino acids of 1051-1069 of SEQ ID NO: 1, at least eight consecutive amino acids of 1121-1139 of SEQ ID NO: 1 or at least eight consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

116. (Currently amended) The composition of claim 114, wherein said BoNT/A peptide has a length of at most 40 amino acids.
117. (Currently amended) The composition of ~~claim 114~~ claim 115, wherein said additional BoNT/A peptides have ~~has~~ a length of at most ~~25~~ 40 amino acids.
118. (Currently amended) The composition of ~~claim 114~~ claim 115, wherein said amino acid sequence of said additional BoNT/A peptide comprises amino acids 981-999 of SEQ ID NO: 1 or an immunoreactive BoNT/A amino acid sequence fragment thereof ~~an amino acid sequence selected from the group: 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 567-~~

~~583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a conservative variant thereof~~

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 981-999 of SEQ ID NO:1 producing an immune response comprises at least eight consecutive amino acids of 981-999 of SEQ ID NO: 1.

119. (Currently amended) The composition of ~~claim 114~~ claim 115, wherein said amino acid sequence of said additional BoNT/A peptide comprises amino acids 1051-1069 of SEQ ID NO: 1 or an immunoreactive BoNT/A amino acid sequence fragment thereof ~~an amino acid sequence selected from the group: 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or an immunoreactive fragment thereof, with the proviso that said BoNT/A peptide is not SEQ ID NO:2~~

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1051-1069 of SEQ ID NO:1 producing an immune response comprises at least eight consecutive amino acids of 1051-1069 of SEQ ID NO: 1.

120. (Currently amended) The composition of ~~claim 114~~ claim 115, wherein said amino acid sequence of said additional BoNT/A peptide comprises amino acids 1121-1139 of SEQ ID NO: 1 or an immunoreactive BoNT/A amino acid sequence fragment thereof ~~an amino acid sequence selected from the group: 445-471 of SEQ ID NO:1, 487-513 of SE ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-~~

~~765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1~~

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1121-1139 of SEQ ID NO:1 producing an immune response comprises at least eight consecutive amino acids of 1121-1139 of SEQ ID NO: 1.

121. (Currently amended) The composition of ~~claim 114~~ claim 115, wherein said amino acid sequence of said additional BoNT/A peptide comprises amino acids 1275-1296 of SEQ ID NO: 1 or an immunoreactive BoNT/A amino acid sequence fragment thereof ~~consists of an amino acid sequence selected from the group: 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1.~~

wherein said immunoreactive BoNT/A amino acid sequence fragment of amino acids 1275-1296 of SEQ ID NO:1 producing an immune response comprises at least eight consecutive amino acids of 1275-1296 of SEQ ID NO: 1.

122. (Canceled)

123. (Currently amended) A method of preparing an anti-BoNT/A antibody, the method comprising the steps of:

- (a) administering to an animal a composition comprising an adjuvant and a BoNT/A peptide of SEQ ID NO: 1 having a length of at most 60 amino acids ~~and~~

wherein said BoNT/A peptide comprises comprising an amino acid sequence selected from the group consisting of~~[[:]] 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1,~~

~~655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a conservative variant or immunoreactive fragment thereof~~ amino acids 491-509 of SEQ ID NO: 1, amino acids 519-537 of SEQ ID NO: 1, amino acids 533-551 of SEQ ID NO: 1, amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 631-649 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 673-691 of SEQ ID NO: 1, 715-733 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 771-789 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 813-831 of SEQ ID NO: 1, amino acids 827-845 of SEQ ID NO: 1 and an immunogenic BoNT/A amino acid sequence fragment thereof;

wherein an immunogenic response is produced by amino acids 491-509 of SEQ ID NO: 1, amino acids 519-537 of SEQ ID NO: 1, amino acids 533-551 of SEQ ID NO: 1, amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 631-649 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 673-691 of SEQ ID NO: 1, 715-733 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 771-789 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 813-831 of SEQ ID NO: 1, amino acids 827-845 of SEQ ID NO: 1 or an immunogenic BoNT/A amino acid sequence fragment thereof; and

wherein said immunogenic BoNT/A amino acid sequence producing an immunogenic response comprises at least six consecutive amino acids of 491-509 of SEQ ID NO: 1, at least six consecutive amino acids of 519-537 of SEQ ID NO: 1, at least six consecutive amino acids of 533-551 of SEQ ID NO: 1, at least six consecutive amino acids of 547-565 of SEQ ID NO: 1, at least six consecutive amino acids of 589-607 of SEQ ID NO: 1, at least six consecutive amino acids of 631-649 of SEQ ID NO: 1, at least six consecutive amino acids of 659-677 of SEQ ID NO: 1, at least six consecutive amino acids of 673-691 of SEQ ID NO: 1, at least six consecutive amino acids of 715-733 of SEQ ID NO: 1, at least six consecutive amino acids of 743-761 of SEQ ID NO: 1, at least six consecutive amino acids of 771-789 of SEQ ID NO: 1,

at least six consecutive amino acids of 785-803 of SEQ ID NO: 1, at least six consecutive amino acids of 813-831 of SEQ ID NO: 1 or at least six consecutive amino acids of 827-845 of SEQ ID NO: 1;

- (b) collecting from said animal a sample containing an antibody or antibody-producing cell; and
- (c) processing said sample to isolate said anti-BoNT/A antibody, ~~with the proviso that said BoNT/A peptide is not SEQ ID NO:2.~~

124. (Currently amended) The method of claim 123, wherein said BoNT/A peptide comprises an amino acid sequence selected from the group consisting of ~~[[:]] 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, and 823-849 of SEQ ID NO:1, or a conservative variant or immunoreactive fragment thereof, with the proviso that said BoNT/A peptide is not SEQ ID NO:2~~ amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1 and an immunogenic BoNT/A amino acid sequence fragment thereof..

wherein said immunogenic BoNT/A amino acid sequence producing an immunogenic response comprises at least six consecutive amino acids of 547-565 of SEQ ID NO: 1, at least six consecutive amino acids of 589-607 of SEQ ID NO: 1, at least six consecutive amino acids of 659-677 of SEQ ID NO: 1, at least six consecutive amino acids of 743-761 of SEQ ID NO: 1 or at least six consecutive amino acids of 785-803 of SEQ ID NO: 1.

125. (Original) The method of claim 123, wherein said BoNT/A peptide has a length of at most 40 amino acids.

126. (Original) The method of claim 123, wherein said BoNT/A peptide has a length of at most 25 amino acids.

127. (Currently amended) The method of claim 123, wherein said BoNT/A peptide comprises an amino acid sequence selected from the group consisting of ~~445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or a conservative variant thereof~~ amino acids 547-565 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1 and a immunogenic BoNT/A amino acid sequence fragment thereof.

wherein said immunogenic BoNT/A amino acid sequence producing an immunogenic response comprises at least six consecutive amino acids of 547-565 of SEQ ID NO: 1 or at least six consecutive amino acids of 785-803 of SEQ ID NO: 1.

128. (Currently amended) The method of claim 123, wherein said BoNT/A peptide comprises an amino acid sequence selected from the group consisting of ~~445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1, or an immunoreactive fragment thereof, with the proviso that said BoNT/A peptide is not~~ SEQ ID NO:2 amino acids 449-467 of SEQ ID NO: 1, amino acids 491-509 of SEQ ID NO: 1, amino acids 519-537 of SEQ ID NO: 1, amino acids 533-551 of SEQ ID NO: 1, amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 631-649 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 673-691 of SEQ ID NO: 1, 715-733 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1, amino acids 771-789 of SEQ ID NO: 1, amino acids 785-803 of SEQ ID NO: 1, amino acids 813-831 of SEQ ID NO: 1 and amino acids 827-845 of SEQ ID NO: 1.

129. (Currently amended) The method of claim 123, wherein said BoNT/A peptide comprises an amino acid sequence selected from the group consisting of ~~445-471 of SEQ ID~~

~~NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1~~ amino acids 547-565 of SEQ ID NO: 1, amino acids 589-607 of SEQ ID NO: 1, amino acids 659-677 of SEQ ID NO: 1, amino acids 743-761 of SEQ ID NO: 1 and amino acids 785-803 of SEQ ID NO: 1.

130. (Currently amended) The method of claim 123, wherein said BoNT/A peptide consists of an amino acid sequence selected from the group consisting of ~~[[:]] 445-471 of SEQ ID NO:1, 487-513 of SEQ ID NO:1, 515-541 of SEQ ID NO:1, 529-555 of SEQ ID NO:1, 543-569 of SEQ ID NO:1, 557-583 of SEQ ID NO:1, 585-611 of SEQ ID NO:1, 599-625 of SEQ ID NO:1, 655-681 of SEQ ID NO:1, 669-695 of SEQ ID NO:1, 683-709 of SEQ ID NO:1, 711-737 of SEQ ID NO:1, 739-765 of SEQ ID NO:1, 767-793 of SEQ ID NO:1, 781-807 of SEQ ID NO:1, 809-835 of SEQ ID NO:1, 823-849 of SEQ ID NO:1, and 837-863 of SEQ ID NO:1~~ amino acids 547-565 of SEQ ID NO: 1 and amino acids 785-803 of SEQ ID NO: 1.

131. (Currently amended) The method of claim 123, wherein said BoNT/A peptide comprises amino acids 785-803 of SEQ ID NO: 1, ~~the amino acid sequence of residues 785-803 of SEQ ID NO: 1 or a conservative variant~~ or immunogenic BoNT/A amino acid sequence fragment thereof

wherein said immunogenic BoNT/A amino acid sequence fragment of amino acids 785-803 of SEQ ID NO: 1 producing an immunogenic response comprises at least six consecutive amino acids of 785-803 of SEQ ID NO: 1.

132. (Original) The method of claim 123, wherein said antibody is polyclonal.
133. (Original) The method of claim 123, wherein said antibody is monoclonal.